09/855,797
Aug 98

=> s recombinase? or integrase? or resolvase? or telomerase?
L1 29845 RECOMBINASE? OR INTEGRASE? OR RESOLVASE? OR TELOMERASE?

=> s ligate or ligates or ligated or ligating or add or adding or added or adds or link or links or linked or linking
L2 3444499 LIGATE OR LIGATES OR LIGATED OR LIGATING OR ADD OR ADDING OR
ADDED OR ADDS OR LINK OR LINKS OR LINKED OR LINKING

=> s l2(5n)(termini or end or ends)
L3 39748 L2(5N)(TERMINI OR END OR ENDS)

=> s l1 and l3
L4 305 L1 AND L3

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5 108 DUP REM L4 (197 DUPLICATES REMOVED)

=> s l5 and py<1998
1 FILES SEARCHED...
3 FILES SEARCHED...
4 FILES SEARCHED...
L6 31 L5 AND PY<1998

=> d l6 ibib abs 1-31

L6 ANSWER 1 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:120936 BIOSIS
DOCUMENT NUMBER: PREV199800120936
TITLE: Telomeres terminating with long complex tandem repeats.
AUTHOR(S): Kamnert, Irene; Lopez, Casimiro C.; Rosen, Monika; Edstrom,
Jan-Erik (1)
CORPORATE SOURCE: (1) Dep. Genetics, Div. Molecular Genetics, Univ. Lund,
Solvegatan 29, SE-223 62 Lund Sweden
SOURCE: Hereditas (Lund), (***Dec., 1997***) Vol. 127, No. 3, pp. 175-180.
ISSN: 0018-0661.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Telomeres of most investigated species terminate with short repeats and are elongated by ***telomerase*** . Short repeats have never been detected in dipteran species which have found other solutions to end a chromosome. Whereas in Drosophila melanogaster retroelements are ***added*** onto the ***termini*** , chironomids have long complex repeats at their chromosome ends. We review evidence that these units are terminal and probably have evolved from short telomeric repeats. In Chironomus pallidivittatus the units have been shown to belong to different subfamilies which have specific inter- and intrachromosomal distribution, the most terminal subfamily of repeats being characterized by pronounced secondary structures for the single strand. The complex repeats are efficiently homogenized both within and between different chromosome ends. Gene conversion is probably an important component in the coordinate evolution of the repeats but it is not known whether it is used for net synthesis of DNA. RNA is used as an intermediate in telomere elongation both by organisms having chromosomes terminating with short repeats and by D. melanogaster. It is therefore interesting that the terminal repeats in chironomids are transcribed.

L6 ANSWER 2 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:92063 BIOSIS
DOCUMENT NUMBER: PREV199800092063
TITLE: Evolutionary links between telomeres and transposable elements.
AUTHOR(S): Pardue, M. L.; Danilevskaya, O. N.; Traverse, K. L.; Lowenhaupt, K.
CORPORATE SOURCE: Dep. Biol., Massachusetts Inst. Technol., Cambridge, MA
02139 USA
SOURCE: Genetica (Dordrecht), (1997) Vol. 100, No. 1-3, pp. 73-84.
ISSN: 0016-6707.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Transposable elements are abundant in the genomes of higher organisms but are usually thought to affect cells only incidentally, by transposing in or near a gene and influencing its expression. Telomeres of Drosophila chromosomes are maintained by two non-LTR retrotransposons, HeT-A and TART. These are the first transposable elements with identified roles in chromosome structure. We suggest that these elements may be evolutionarily related to ***telomerase*** ; in both cases an enzyme extends the ***end*** of a chromosome by ***adding*** DNA copied from an RNA template. The evolution of transposable elements from chromosomal replication mechanisms may have occurred multiple times, although in other organisms the new products have not replaced the endogenous ***telomerase*** , as they have in Drosophila. This is somewhat reminiscent of the oncogenes that have arisen from cellular genes. Perhaps the viruses that carry oncogenes have also arisen from cellular genetic systems.

L6 ANSWER 3 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:80639 BIOSIS
DOCUMENT NUMBER: PREV199800080639
TITLE: ***Telomerase*** activity in human leukemic cell lines is inhibited by antisense pentadecadeoxynucleotides targeted against c-myc mRNA.
AUTHOR(S): Fujimoto, Kohtaro; Takahashi, Morinobu (1)
CORPORATE SOURCE: (1) Dep. Cell. Mol. Biol., Cancer Res. Inst., Kanazawa
Univ., 13-1 Takaramachi, Kanazawa 920 Japan
SOURCE: Biochemical and Biophysical Research Communications, (***Dec. 29, 1997***) Vol. 241, No. 3, pp. 775-781.
ISSN: 0006-291X.
DOCUMENT TYPE: Article
LANGUAGE: English
AB ***Telomerase*** is a ribonucleoprotein complex that is thought to ***add*** telomeric repeats to the ***ends*** of chromosomes during the replicative phase of the cell cycle. We tested the hypothesis that proto-oncogene c-myc plays an essential role in the regulation of ***telomerase*** activity in vertebrate cells by exposing three human leukemic cell lines, HL60, U937, and K562, to 15-mer antisense c-myc oligonucleotides. All the treated cells showed a profound decrease in ***telomerase*** activity after c-myc antisense oligomer treatment, whereas cells treated with c-myc sense oligomers showed essentially no change in ***telomerase*** activity.

L6 ANSWER 4 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:80638 BIOSIS
DOCUMENT NUMBER: PREV199800080638
TITLE: Inhibition of ***telomerase*** activity by PKC inhibitors in human nasopharyngeal cancer cells in culture.
AUTHOR(S): Ku, Wei-Chi; Cheng, Ann-Joy; Wang, Tzu-Chien V. (1)
CORPORATE SOURCE: (1) Dep. Mol. Cell. Biol., Coll. Med., Chang Gung Univ.,
Kwei-San, Tao-Yuan Taiwan
SOURCE: Biochemical and Biophysical Research Communications, (***Dec. 29, 1997***) Vol. 241, No. 3, pp. 730-736.
ISSN: 0006-291X.
DOCUMENT TYPE: Article
LANGUAGE: English
AB ***Telomerase*** is a specialized ribonucleoprotein polymerase that ***adds*** hexanucleotides (TTAGGG) onto human chromosomal ***ends*** . The expression of ***telomerase*** activity has been associated with cell immortalization and the malignant phenotype in most cancers. How the ***telomerase*** activity is regulated in cancer cells is presently not known. In this work, the effects of cell cycle blockers, DNA damaging agents, TopII inhibitors and proteins kinase inhibitors on the ***telomerase*** activity were examined in cultured nasopharyngeal

carcinoma cells NPC-076. Agents which interfere with tubulin assembly (Taxol and vinblastine) and agents which arrest cells at S phase (methotrexate and 5-fluorouracil) did not inhibit ***telomerase*** activity of treated cells. Agents which damage DNA (cisplatin, methyl methanesulfonate, and UV radiation) and TopII inhibitors (etoposide and daunorubicin) also did not inhibit ***telomerase*** activity of treated cells. Among the protein kinase inhibitors examined, no significant inhibition of ***telomerase*** activity was observed with cells treated with quercetin, H-89, or herbimycin A. On the other hand, two protein kinase C (PKC) inhibitors (bisindolylmaleimide I and H-7) were found to produce a big inhibition of ***telomerase*** activity in treated cells. Staurosporine produced a moderate inhibition, and sphingosine had a small inhibitory effect. The inhibition of ***telomerase*** activity by PKC inhibitors appears to be specific since the treated cells were mostly viable (i.e., greater than 75%) and still retained significant levels of protein synthesis capability. These results implicate that protein kinase C is involved in the regulation of ***telomerase*** activity in vivo.

L6 ANSWER 5 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:6090 BIOSIS
DOCUMENT NUMBER: PREV199800006090
TITLE: Functionally interacting ***telomerase*** RNAs in the yeast ***telomerase*** complex.
AUTHOR(S): Prescott, John; Blackburn, Elizabeth H. (1)
CORPORATE SOURCE: (1) Dep. Microbiology Immunol., Univ. Calif., San Francisco, CA 94143-0414 USA
SOURCE: Genes & Development, (***Nov. 1, 1997***) Vol. 11, No. 21, pp. 2790-2800.
ISSN: 0890-9369.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The ribonucleoprotein (RNP) enzyme ***telomerase*** from Saccharomyces cerevisiae ***adds*** telomeric DNA to chromosomal ***ends*** in short increments both in vivo and in vitro. Whether or not ***telomerase*** functions as a multimer has not been addressed previously. Here we show, first, that following polymerization, the ***telomerase*** RNP remains stably bound to its telomeric oligonucleotide reaction product. We then exploit this finding and a previously reported mutant ***telomerase*** RNA to demonstrate that, unexpectedly, the S. cerevisiae ***telomerase*** complex contains at least two functionally interacting RNA molecules that both act as templates for DNA polymerization. Here, functional ***telomerase*** contains at least two active sites.

L6 ANSWER 6 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:5849 BIOSIS
DOCUMENT NUMBER: PREV199800005849
TITLE: Isolation of a candidate human ***telomerase*** catalytic subunit gene, which reveals complex splicing patterns in different cell types.
AUTHOR(S): Kilian, Andrzej (1); Bowtell, David D. L.; Abud, Helen E.; Hime, Gary R.; Venter, Deon J.; Keese, Paul K.; Duncan, Emma L.; Reddel, Roger R.; Jefferson, Richard A.
CORPORATE SOURCE: (1) CAMBIA, GPO Box 3200, Canberra, ACT 2601 Australia
SOURCE: Human Molecular Genetics, (***Nov., 1997***) Vol. 6, No. 12, pp. 2011-2019.
ISSN: 0964-6906.
DOCUMENT TYPE: Article
LANGUAGE: English
AB ***Telomerase*** is a multicomponent reverse transcriptase enzyme that ***adds*** DNA repeats to the ***ends*** of chromosomes using its RNA component as a template for synthesis. ***Telomerase*** activity is detected in the germline as well as the majority of tumors and immortal cell lines, and at low levels in several types of normal cells. We have cloned a human gene homologous to a protein from Saccharomyces cerevisiae and Euplotes aediculatus that has reverse transcriptase motifs and is thought to be the catalytic subunit of ***telomerase*** in those species. This gene is present in the human genome as a single copy sequence with a dominant transcript of apprx 4 kb in a human colon cancer cell line, LIM1215. The cDNA sequence was determined using clones from a LIM1215 cDNA library and by RT-PCR, cRACE and 3'RACE on mRNA from the same source. We show that the gene is expressed in several normal tissues, ***telomerase*** -positive post-crisis (immortal) cell lines and various tumors but is not expressed in the majority of normal tissues analyzed, pre-crisis (non-immortal) cells and ***telomerase*** -negative immortal (ALT) cell lines. Multiple products were identified by RT-PCR using primers within the reverse transcriptase domain. Sequencing of these products suggests that they arise by alternative splicing. Strikingly, various tumors, cell lines and even normal tissues (colonic crypt and testis) showed considerable differences in the splicing patterns. Alternative splicing of the ***telomerase*** catalytic subunit transcript may be important for the regulation of ***telomerase*** activity and may give rise to proteins with different biochemical functions.

L6 ANSWER 7 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:319779 BIOSIS
DOCUMENT NUMBER: PREV199799610267
TITLE: Human immunodeficiency virus type 1 preintegration complexes: Studies of organization and composition.
AUTHOR(S): Miller, Michael D.; Farnet, Chris M.; Bushman, Frederic D. (1)
CORPORATE SOURCE: (1) Infectious Disease Lab., Salk Inst. Biol. Studies, 10010 N. Torrey Pines Rd., La Jolla, CA 92037 USA
SOURCE: Journal of Virology, (1997) Vol. 71, No. 7, pp. 5382-5390.
ISSN: 0022-538X.
DOCUMENT TYPE: Article
LANGUAGE: English
AB We have investigated the organization and function of human immunodeficiency virus type 1 (HIV-1) preintegration complexes (PICs), the large nucleoprotein particles that carry out cDNA integration in vivo. PICs can be isolated from HIV-1-infected cells, and such particles are capable of carrying out integration reactions in vitro. We find that although the PICs are large, the cDNA must be condensed to fit into the measured volume. The ***ends*** of the cDNA are probably ***linked*** by a protein bridge, since coordinated joining of the two ends is not disrupted by cleaving the cDNA internally with a restriction enzyme. cDNA ends in PICs were protected from digestion by added exonucleases, probably due to binding of proteins. The intervening cDNA, in contrast, was susceptible to attack by endonucleases. Previous work has established that the virus-encoded ***integrase*** protein is present in PICs, and we have reported recently that the host protein HMG I(Y) is also present. Here we report that the viral matrix and reverse transcriptase (RT) proteins also cofractionated with PICs through several steps whereas capsid and nucleocapsid proteins dissociated. These data support a model of PIC organization in which the cDNA is condensed in a partially disassembled remnant of the viral core, with proteins tightly associated at the apposed cDNA ends but loosely associated with the intervening cDNA. In characterizing the structure of the cDNA ends, we found that the U5 DNA ends created by RT were ragged, probably due to the terminal transferase activity of RT. Only molecules correctly cleaved by ***integrase*** protein at the 3' ends were competent to integrate, suggesting that one role for terminal cleavage by ***integrase*** may be to create a defined end at otherwise heterogeneous cDNA termini.

L6 ANSWER 8 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:292822 BIOSIS
DOCUMENT NUMBER: PREV199799592025
TITLE: Multiple pathways to cellular senescence: Role of ***telomerase*** repressors.
AUTHOR(S): Oshimura, M. (1); Barrett, J. C.
CORPORATE SOURCE: (1) Dep. Molecular Cell Genetics, Sch. Life Sci.,

Fac.
Med., Tottori Univ. Nishimachi 86, Yonago, Tottori 683 Japan
SOURCE: European Journal of Cancer, (1997) Vol. 33, No. 5, pp. 710-715.
ISSN: 0959-8049.
DOCUMENT TYPE: General Review
LANGUAGE: English
AB Telomeres progressively shorten with age in somatic cells in culture and in vivo because DNA replication results in the loss of sequences at the 5' ends of double-stranded DNA. Whereas somatic cells do not express the enzyme, ***telomerase*** , which ***adds*** repeated telomere sequences to chromosome ***ends*** , ***telomerase*** activity is detected in immortalised and tumour cells in vitro and in primary tumour tissues. This represents an important difference between normal cells and cancer cells, suggesting that telomere shortening causes cellular senescence. Hybrids between immortal cells and normal cells senesce, indicating that immortal cells have lost, mutated or inactivated genes that are required for the programme of senescence in normal cells. Genes involved in the senescence programme have been mapped to over ten different genetic loci using microcell fusion to introduce human chromosomes and restore the senescence programme. Multiple pathways of cellular senescence have also been demonstrated by chromosome transfer, indicating that the functions of the mapped senescence genes are probably different. One possibility is that one or more of these senescence genes may suppress ***telomerase*** activity in immortal cells, resulting in telomere shortening and cellular senescence. To test this hypothesis, ***telomerase*** activity and the length of terminal restriction fragments (TRFs) have been examined in microcell hybrids. Re-introduction of a normal chromosome 3 into the renal cell carcinoma cell line RCC23, which has the short arm of chromosome 3, restored cellular senescence. The loss of indefinite growth potential was associated with the loss of ***telomerase*** activity and shortening of telomeres in the RCC cells containing the introduced chromosome 3. However, microcell hybrids that escaped from senescence and microcell hybrids with an introduced chromosome 7 or 11 maintained telomere lengths and ***telomerase*** activity similar to the parental RCC23. Thus, restoration of cellular senescence by chromosome 3 is associated with repression of ***telomerase*** function in RCC cells. This evidence suggests that ***telomerase*** suppression is one of several pathways involved in immortalisation.

L6 ANSWER 9 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:163514 BIOSIS
DOCUMENT NUMBER: PREV199799462717
TITLE: ***Telomerase*** RNA mutations in Saccharomyces cerevisiae alter ***telomerase*** action and reveal nonprocessivity in vivo and in vitro.
AUTHOR(S): Prescott, John; Blackburn, Elizabeth H. (1)
CORPORATE SOURCE: (1) Dep. Microbiol. Immunol., Univ. California San Francisco, San Francisco, CA 94143-0414 USA
SOURCE: Genes & Development, (1997) Vol. 11, No. 4, pp. 528-540.
ISSN: 0890-9369.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The ribonucleoprotein enzyme ***telomerase*** ***adds*** telomeric DNA to chromosomal ***ends*** . In most eukaryotes the telomeric repeat units are repeated precisely, consistent with the action of a ***telomerase*** that faithfully copies its RNA template. In contrast, Saccharomyces cerevisiae telomeric repeats are degenerate, suggesting that its ***telomerase*** has unusual mechanistic properties. We mutated the S. cerevisiae ***telomerase*** RNA (TLC1) with a series of 3-base (GUG) substitutions in and next to the 17-nucleotide templating domain. All mutant ***telomerases*** were active in TLC1/tlc1 diploids and synthesized patterns of mixed wild-type and mutant telomeric repeats into telomeric DNA, consistent with nonprocessive action. ***Telomerase*** isolated from cells containing each mutated tlc1 allele by itself had altered reaction properties in vitro. One mutant template enzyme, 476GUG, was active in vivo and in vitro in the presence of wild-type TLC1 RNA but lacked detectable activity in its absence. Haploid tlc1-476GUG cells containing only this mutant tlc1 allele underwent senescence. Other tlc1 template region mutations allowed maintenance of shortened telomeres in vivo but altered specific enzymatic properties of ***telomerase*** in vitro, including induction of primer-template slippage (472GUG) or alteration of the 5' boundary of the template (467GUG). These data demonstrate that ***telomerase*** RNA bases influence enzyme activity profoundly, suggesting that their roles are not confined to serving simply as the template for this specialized reverse transcriptase.

L6 ANSWER 10 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:163488 BIOSIS
DOCUMENT NUMBER: PREV199799462691
TITLE: The yeast site-specific ***recombinase*** Flp mediates alcoholysis and hydrolysis of the strand cleavage product: Mimicking the strand-joining reaction with non-DNA nucleophiles.
AUTHOR(S): Knudsen, Birgitta R.; Dahlstrom, Kristina; Westergaard, Ole; Jayaram, Makkuni (1)
CORPORATE SOURCE: (1) Dep. Microbiol., Univ. Texas, Austin, TX 78712 USA
SOURCE: Journal of Molecular Biology, (1997) Vol. 266, No. 1, pp. 93-107.
ISSN: 0022-2836.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The yeast site-specific ***recombinase*** Flp is covalently linked to DNA via a 3'-phosphotyrosyl bond during the strand-breakage step of recombination. We show that this phosphotyrosyl diester bond formed between Flp and DNA can serve as the target for alcoholysis or hydrolysis in an Flp-assisted reaction. Flp does not mediate alcoholysis of the labile phosphodiester bond within the DNA chain under our assay conditions. The body of available evidence supports the notion that the alcoholysis/hydrolysis reaction is mechanistically analogous to the strand-joining step of the recombination pathway. The only difference is that the DNA 5'-hydroxyl group that acts as the nucleophile during recombination is substituted by a non-DNA nucleophile. We find that the alcoholysis reaction occurs only within the normal cleavage complex produced by the "shared active site" assembled at the interface of two Flp monomers. Unlike the strand-joining reaction, alcoholysis does not occur on an activated DNA substrate ***linked*** at its 3'-phosphate ***end*** to a short tyrosyl peptide (not to the full-length Flp), and bound non-covalently by a Flp monomer. However, even in this substrate that mimics the strand-cleaved state, the joining reaction is competitively inhibited by a polyhydric alcohol such as glycerol.

L6 ANSWER 11 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:66449 BIOSIS
DOCUMENT NUMBER: PREV199799365652
TITLE: ***Telomerase*** activity concentrates in the mitotically active segments of human hair follicles.
AUTHOR(S): Ramirez, Ruben D.; Wright, Woodring E.; Shay, Jerry W.; Taylor, R. Stan (1)
CORPORATE SOURCE: (1) Dep. Dermatology, Univ. Texas Southwestern Med. Cent., 5323 Harry Hines Boulevard, Dallas, TX 75235-9069 USA
SOURCE: Journal of Investigative Dermatology, (1997) Vol. 108, No. 1, pp. 113-117.
ISSN: 0022-202X.
DOCUMENT TYPE: Article
LANGUAGE: English
AB ***Telomerase*** is a ribonucleoprotein enzyme capable of ***adding*** hexanucleotide repeats onto the ***ends*** of linear chromosomal DNA. Whereas normal somatic cells with a limited replicative capacity fail to express ***telomerase*** activity, most immortal eukaryotic cells do. Cells of renewal tissues (e.g., skin, intestine, blood) require an extensive proliferative capacity. Some cells in such renewal tissues also express ***telomerase*** activity, most likely to prevent rapid erosion of their telomeres during cell proliferation. In

this study. we measured the levels of ***telomerase*** activity in dissected compartments of the human hair follicle: hair shaft, gland-containing fragment, upper intermediate fragment (where it is thought undifferentiated stem cells reside), lower intermediate fragment, and in the bulb-containing fragment (an area with high mitotic activity containing a more differentiated pool of keratinocytes). In anagen follicles, high levels of ***telomerase*** activity were found almost exclusively in the bulb-containing fragment of the follicles, with low levels of ***telomerase*** in the bulge area (intermediate fragments) and gland-containing fragment. In comparison, catagen follicles had low levels of ***telomerase*** activity in the bulb-containing fragments as well as in other compartments. Such observations indicate that, in anagen hair follicles, the fragments containing cells actively dividing (e.g., transient amplifying cells) express ***telomerase*** activity, whereas fragments containing cells with low mitotic activity, for example, quiescent stem cells, express low levels of ***telomerase*** activity.

L6 ANSWER 12 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:64112 BIOSIS
DOCUMENT NUMBER: PREV199799363315
TITLE: The anchor site of ***telomerase*** from Euplotes aediculatus revealed by photo-cross-linking to single- and double-stranded DNA primers.
AUTHOR(S): Hammond, Philip W.; Lively, Tricia N.; Cech, Thomas R. (1)
CORPORATE SOURCE: (1) Campus Box 215, University Colorado, Boulder, CO 80309-0215 USA
SOURCE: Molecular and Cellular Biology, (1997) Vol. 17, No. 1, pp. 296-308.
ISSN: 0270-7306.
DOCUMENT TYPE: Article
LANGUAGE: English
AB ***Telomerase*** is a ribonucleoprotein enzyme that ***adds*** telomeric sequence repeats to the ***ends*** of linear chromosomes. In vitro, ***telomerase*** has been observed to add repeats to a DNA oligonucleotide primer in a processive manner, leading to the postulation of a DNA anchor site separate from the catalytic site of the enzyme. We have substituted photoreactive 5-iododeoxypyrimidines into the DNA oligonucleotide primer d(T-4G-4T-4G-4T-4G-2) and, upon irradiation, obtained cross-links with the anchor site of ***telomerase*** from Euplotes aediculatus nuclear extract. No cross-linking occurred with a primer having the same 5' end and a nontelomeric 3' ***end*** . These cross- ***links*** were shown to be between the DNA primer and (i) a protein moiety of approximately 130 kDa and (ii) U51-U52 of the ***telomerase*** RNA. The cross-linked primer could be extended by ***telomerase*** in the presence of (alpha-32P)dGTP, thus indicating that the 3' end was bound in the enzyme active site. The locations of the cross-links within the single-stranded primers were 20 to 22 nucleotides upstream of the 3' end, providing a measure of the length of DNA required to span the ***telomerase*** active and anchor sites. When the single-stranded primers are aligned with the G-rich strand of a Euplotes telomere, the cross-linked nucleotides correspond to the duplex region. Consistent with this finding, a cross-link to ***telomerase*** was obtained by substitution of 5-iododeoxycytidine into the CA strand of the duplex region of telomere analogs. We conclude that the anchor site in the apprx 130-kDa protein can bind duplex as well as single-stranded DNA, which may be critical for its function at chromosome ends. Quantitation of the processivity with single-stranded DNA primers and double-stranded primers with 3' tails showed that only 60% of the primer remains bound after each repeat addition.

L6 ANSWER 13 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:41654 BIOSIS
DOCUMENT NUMBER: PREV199799333642
TITLE: Human ***telomerase*** inhibition by 7-deaza-2'-deoxypurine nucleoside triphosphates.
AUTHOR(S): Fletcher, Terace M.; Salazar, Miguel; Chen, Shih-Fong (1)
CORPORATE SOURCE: (1) Cancer Therapy, Res. Cent., Inst. Drug Development, 14960 Omicron Dr., San Antonio, TX 78245 USA
SOURCE: Biochemistry, (1996) Vol. 35, No. 49, pp. 15611-15617.
ISSN: 0006-2960.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Telomeres play an important role in chromosome organization and stability. Human ***telomerase*** is a terminal transferase that ***adds*** TTAGGG units onto the telomere ***end*** . In general, ***telomerase*** activity is not detected in normal somatic cells but is present in immortalized cells. Consequently, ***telomerase*** might be a selective target for cancer chemotherapy. Using cell-free biochemical ***telomerase*** assay, we have found that 7-deaza-2'-deoxyguanosine-5'-triphosphate (7-deaza-dGTP) and 7-deaza-2'-deoxyadenosine-5'-triphosphate (7-deaza-dATP) were potent ***telomerase*** inhibitors. The concentrations of inhibitors in which 50% of the ***telomerase*** activity was inhibited (IC-50 values) were 11 and 8 mu-M for 7-deaza-dGTP and 7-deaza-dATP, respectively. Additional studies show that both 7-deaza-dGTP and 7-deaza-dATP were also incorporated into telomeric DNA by ***telomerase*** . However, incorporation of 7-deaza-dATP or 7-deaza-dGTP results in a telomeric ladder that is prematurely shortened. No difference in the number or position of pause sites were observed when 7-deaza-dATP was compared to dATP as substrates. On the other hand, both a shift and an increase in pause sites was observed when dGTP was replaced by 7-deaza-dGTP. Incorporation of 7-deaza nucleotides by ***telomerase*** may be used as a tool for the study of ***telomerase*** mechanism and function. In addition, this may be a novel approach in the design of new ***telomerase*** inhibitors.

L6 ANSWER 14 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1996:334714 BIOSIS
DOCUMENT NUMBER: PREV199699057070
TITLE: Cell cycle-dependent modulation of ***telomerase*** activity in tumor cells.
AUTHOR(S): Zhu, Xueli; Kumar, Rakesh; Mandal, Mahitoshi; Sharma, Neeta; Sharma, Harsh W.; Dhingra, Urvashi; Sokoloski, John A.; Hsiao, Rongshen; Narayanan, Ramaswamy (1)
CORPORATE SOURCE: (1) Div. Oncol., Roche Res. Cent., Hoffman-La Roche Inc., 340 Kingsland St., Nutley, NJ 07110 USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1996) Vol. 93, No. 12, pp. 6091-6095.
ISSN: 0027-8424.
DOCUMENT TYPE: Article
LANGUAGE: English
AB ***Telomerase*** is a ribonucleoprotein complex that is thought to ***add*** telomeric repeats onto the ***ends*** of chromosomes during the replicative phase of the cell cycle. We tested this hypothesis by arresting human tumor cell lines at different stages of the cell cycle. Induction of quiescence by serum deprivation did not affect ***telomerase*** activity. Cells arrested at the G-1/S phase of the cell cycle showed similar levels of ***telomerase*** to asynchronous cultures; progression through the S phase was associated with increased ***telomerase*** activity. The highest level of ***telomerase*** activity was detected in S-phase cells. In contrast, cells arrested at G-2/M phase of the cell cycle were almost devoid of ***telomerase*** activity. Diverse cell cycle blockers, including transforming growth factor beta-1 and cytotoxic agents, also caused inhibition of ***telomerase*** activity. These results establish a direct link between ***telomerase*** activity and progression through the cell cycle.

L6 ANSWER 15 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1995:488167 BIOSIS
DOCUMENT NUMBER: PREV199598502467
TITLE: DNA ***recombinase*** activity of eukaryotic DNA topoisomerase I: Effects of camptothecin and other inhibitors.
AUTHOR(S): Pommier, Yves (1); Jenkins, Jeffrey; Kohlhagen, Glenda; Leteurtre, Francois
CORPORATE SOURCE: (1) Lab. Molecular Pharmacol., Dev.

Therapeutics Program,
Div. Cancer Treatment, Natl. Cancer Inst., Build. 37, Room 5C25, Natl. Inst. Health, Bethesda, MD 20892-4255 USA
SOURCE: Mutation Research, (1995) Vol. 337, No. 2, pp. 135-145.
ISSN: 0027-5107.
DOCUMENT TYPE: Article
LANGUAGE: English
AB DNA oligonucleotides containing a strong topoisomerase I cleavage site were used to study the DNA cleavage and strand transferase activities of calf thymus topoisomerase I (top1) in the absence and presence of camptothecin. A partially single-stranded oligonucleotide with only two nucleotides on the 3' side of the cleavage site (positions +1 and +2) was cleaved at the same position as the corresponding duplex oligonucleotide. However, cleavage in the absence of camptothecin was more pronounced than in the duplex oligonucleotide and was only partially reversible in the presence of 0.5 M NaCl, consistent with release of the dinucleotide 3' to the top1 break. Another reaction took place generating a larger DNA fragment which resulted from religation (strand transfer) of the 5'-hydroxyl terminus of the non-scissile DNA strand to the 3' ***end*** of the top1- ***linked*** oligonucleotide after loss of the +1 and +2 nucleotides. Top1 religation activity appeared efficient since only the last 5' base of the single-stranded DNA acceptor was complementary to the 3' tail of the donor DNA. Religation was not detectable with a double-stranded DNA acceptor, which is consistent with the persistence of top1-induced DNA double-strand breaks in camptothecin-treated cells. Camptothecin and other top1 inhibitors enhanced cleavage in both the partially single-stranded and the duplex oligonucleotides, indicating that they did not inhibit the induction of top1-mediated DNA cleavage but primarily blocked the religation step of the enzyme catalytic cycle. The top1 DNA strand transferase activity was reversibly inhibited by camptothecin and several derivatives, as well as saintopin. These results are discussed in terms of camptothecin-induced DNA recombinations.

L6 ANSWER 16 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1995:411714 BIOSIS
DOCUMENT NUMBER: PREV199598426014
TITLE: Telomere dynamics and ***telomerase*** activation in tumor progression: Prospects for prognosis and therapy.
AUTHOR(S): Healy, Kim Coleman
CORPORATE SOURCE: Dep. Pharmacol., Yale Univ. Sch. Med., 47 College St.,
Suite 227, New Haven, CT 06510 USA
SOURCE: Oncology Research, (1995) Vol. 7, No. 3-4, pp. 121-130.
ISSN: 0965-0407.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Eukaryotic telomeres provide a reservoir of redundancy to compensate for incomplete replication of chromosome ends. In multicellular eukaryotes, they are eroded by a varying number of base pairs at every cell division. When telomere repeats are critically shortened, DNA damage response pathways involving p53 (and in some cell types retinoblastoma protein) are invoked, leading to "M1 senescence" in normal cells; cancer cells, which frequently lack normal p53 and RB functions, often develop chromosomal instability leading to telomeric associations, ring chromosomes, and breakage-fusion-bridge cycles. These consequences of telomere erosion exert selection pressure for activation of the ribonucleoprotein enzyme ***telomerase*** , which ***adds*** new telomeric repeats at chromosome ***ends*** , and in vertebrates normally is active only in the germ line and the early embryo. Somatic cells that reactivate ***telomerase*** in vitro or in vivo become immortal. ***Telomerase*** activity has been found in many advanced and metastatic human cancers, suggesting that ***telomerase*** -dependent M2 immortalization may contribute to metastatic potential. When mammalian ***telomerases*** are isolated and their genes cloned and sequenced, the localization of ***telomerase*** expression in tumors may provide prognostic indicators of metastatic potential. The abrogation of ***telomerase*** function by pharmacological inhibition, genetic disruption, or repression of gene expression is a potential avenue of antimetastatic therapy.

L6 ANSWER 17 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1995:409172 BIOSIS
DOCUMENT NUMBER: PREV199598423472
TITLE: Runaway telomere elongation caused by ***telomerase*** RNA gene mutations.
AUTHOR(S): McEachern, Michael J.; Blackburn, Elizabeth H.
CORPORATE SOURCE: Dep. Microbiology Immunology, Box 0414, Univ. Calif. at San
Francisco, San Francisco, CA 94143 USA
SOURCE: Nature (London), (1995) Vol. 376, No. 6539, pp. 403-409.
ISSN: 0028-0836.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The ribonucleoprotein enzyme ***telomerase*** ***adds*** telomeric DNA onto chromosome ***ends*** and is normally regulated so that telomeric DNA lengths are kept within defined bounds. In the ***telomerase*** RNA gene from the yeast Kluyveromyces lactis, specific mutations that alter telomeric DNA sequences result in telomeres elongating to up to 100 times their normal length and impair cell growth. Some mutations cause immediate elongation whereas others behave like genetic time bombs, causing elongation only after a latent period of hundreds of generations.

L6 ANSWER 18 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1995:107483 BIOSIS
DOCUMENT NUMBER: PREV199598121783
TITLE: Architecture of ***telomerase*** RNA.
AUTHOR(S): Bhattacharyya, Anamitra; Blackburn, Elizabeth H. (1)
CORPORATE SOURCE: (1) Dep. Microbiol. Immunol., Box 0414, Univ. California,
San Francisco, CA 94143 USA
SOURCE: EMBO (European Molecular Biology Organization) Journal,
(1994) Vol. 13, No. 23, pp. 5721-5731.
ISSN: 0261-4189.
DOCUMENT TYPE: Article
LANGUAGE: English
AB ***Telomerase*** , an essential ribonucleoprotein reverse transcriptase, ***adds*** telomeric DNA to the ***ends*** of eukaryotic chromosomes. We examined the conformational properties of the naked RNA moiety of ***telomerase*** from two related ciliates, Tetrahymena thermophila and Glaucoma chattoni. As well as finding evidence for features proposed previously on the basis of phylogenetic comparisons, novel conserved structural properties were revealed. Specifically, although the region around helix III was previously proposed to form a pseudoknot, our results indicate that in the naked RNA this region maintains a level of 'plasticity', probably in an equilibrium favoring one of two helices. In addition, these studies reveal that the templating domain is not entirely single-stranded as previously proposed, but is ordered due to constraints imposed by other parts of the RNA. Finally, our results suggest that the GA bulge in helix IV may introduce a structurally conserved kink. We now propose a 'two-domain' structure for the ***telomerase*** RNA based on function: one conformationally flexible domain, which includes the template and the region around helix III, involved with enzymatic function, and a second largely helical domain, including helices I and IV and the proposed kink, which may serve as a scaffold for protein binding.

L6 ANSWER 19 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1993:186264 BIOSIS
DOCUMENT NUMBER: PREV199395096714
TITLE: Acquisition of telomere repeat sequences by transfected DNA
integrated at the site of a chromosome break.
AUTHOR(S): Murnane, John P. (1); Yu, Loh-Chung
CORPORATE SOURCE: (1) Lab. Radiology Environmental Health, Univ. California,
San Francisco, CA 94143-0750 USA
SOURCE: Molecular and Cellular Biology, (1993) Vol. 13, No. 2, pp.
977-983.

ISSN: 0270-7306.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Previous analysis of plasmid DNA transfected into 108 cell clones demonstrated extensive polymorphism near the integration site in one clone. This polymorphism was apparent by Southern blot analysis as diffuse bands that extended over 30 kb. In the present study, nucleotide sequence analysis of cloned DNA from the integration site revealed telomere repeat sequences at the ends of the integrated plasmid DNA. The telomere repeat sequences at one end were located at the junction between the plasmid and cell DNA. The telomere repeat sequences at the other end were located in the opposite orientation in the polymorphic region and were shown by digestion with BAL 31 to be at the end of the chromosome. Telomere repeat sequences were not found at this location in the plasmid or parent cell DNA. Although the repeat sequences may have been acquired by recombination, a more likely explanation is that they were ***added*** to the ***ends*** of the plasmid by telomere before integration. Comparison of the cell DNA before abd after integration revealed that a chromosome break had occurred at the integration site, which was shown by fluorescent in situ hybridization to be located near the telomere of chromosome 13. These results demonstrate that chromosome breakage and rearrangement can result in interstitial telomere repeat sequences within the human genome. These sequences could promote genomic instability, because short repeat sequences can be recombinational hotspots. The results also show that DNA rearrangements involving telomere repeat sequences can be associated with chromosome breaks. The introduction of telomere repeat sequences at spontaneous or ionizing radiation-induced DNA strand breaks may therefore also be a mechanism of chromosome fragmentation.

L6 ANSWER 20 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1993:9247 BIOSIS
DOCUMENT NUMBER: PREV199395009247
TITLE: Endoxyloglucan transferase, a novel class of glycosyltransferase that catalyzes transfer of a segment of xyloglucan molecule to another xyloglucan molecule.
AUTHOR(S): Nishitani, Kazuhiko (1); Tominaga, Rumi
CORPORATE SOURCE: (1) Dep. Biology, Coll. Liberal Arts, Kagoshima Univ., Kagoshima 890 Japan
SOURCE: Journal of Biological Chemistry, (1992) Vol. 267, No. 29, pp. 21058-21064.
ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Xyloglucans are the major component of plant cell walls and bind tightly to the surface of individual cellulose microfibrils, thereby cross-linking them into a complex polysaccharide network of the cell wall. The cleavage and reconnection of xyloglucan cross-links are considered to play the leading role during chemical processes essential for wall expansion and, therefore, cell growth and differentiation. Although it is hypothesized that some transglycosylation is involved in these chemical processes, the enzyme responsible for the reaction was not identified. We have now purified a novel class of endo-type glycosyltransferase to apparent homogeneity from the extracellular space or the cell wall of the epicotyls of Vigna angularis, a bean plant. The enzyme is a glycoprotein with a molecular mass of about 33 kDa. The enzyme catalyzes both 1) endo-type splitting of a xyloglucan molecule and 2) ***linking*** of a newly generated reducing ***end*** of the xyloglucan to the nonreducing end of another xyloglucan molecule, thereby mediating the transfer of a large segment of the xyloglucan to another xyloglucan molecule. The transferase exhibits no glycosidase or glycanase activity. Substrate specificity of the enzyme was investigated using several polysaccharides with different glycosidic linkages as donor substrates and pyridylamino oligosaccharides as acceptor substrates, in which the reducing end of the carbohydrate was tagged with a fluorescent group. The enzyme required a basic xyloglucan structure, i.e. a beta-(1 fwdarw 4)-glucosyl backbone with xylosyl side chains, for both acceptor and donor activity. Galactosyl or fucosyl side chains on the main chain were not required for the acceptor activity. The enzyme exhibited higher reaction rates when xyloglucans with higher M-r were used as donor substrates. Xyloglucans smaller than 10 kDa were no longer the donor substrate. On the other hand, pyridylamino heptasaccharide acted as a good acceptor as did xyloglucan polymers. Based on these results we propose to designate this novel enzyme a xyloglucan: xyloglucanotransferase, to be abbreviated endo-xyloglucan transferase (EXT) or xyloglucan ***recombinase*** . This enzyme is the first enzyme identified that mediates the transfer of a high M-r segment between polysaccharide molecules to generate chimeric polymers. We conclude that endo-xyloglucan transferase functions as a reconnecting enzyme for xyloglucans and is involved in the interweaving or reconstruction of cell wall matrix, which is responsible for chemical creepage that leads to morphological changes in the cell wall.

L6 ANSWER 21 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1992:27165 BIOSIS
DOCUMENT NUMBER: BA93:16440
TITLE: ***RESOLVASE*** -CATALYSED REACTIONS BETWEEN RES SITES DIFFERING IN THE CENTRAL DINUCLEOTIDE OF SUBSITE I.
AUTHOR(S): STARK W M; GRINDLEY N D F; HATFULL G F; BOOCOCK M R
CORPORATE SOURCE: INST. GENETICS, UNIV. GLASGOW, CHURCH ST., GLASGOW G11 5JS, UK.
SOURCE: EMBO (EUR MOL BIOL ORGAN) J, (1991) 10 (11), 3541-3548.
CODEN: EMJODG. ISSN: 0261-4189.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB The ***resolvase*** -catalysed reaction between two res sites in a circular DNA substrate normally gives two circular recombination products linked in a two-noded catenane. Homology between the two res sites at the central overlap dinucleotide of subsite I is important for recombination. Reaction between res sites differing at one position in the central dinucleotide (AC .times. AT) gave a low yield of recombinants containing mismatched base-pairs, but gave large amounts of a non-recombinant four-noded knot. This result was predicted by a 'simple rotation' model for strand exchange. The mismatch is evidently recognized only after commitment to an initial 180.degree. rotation of the ***resolvase*** - ***linked*** DNA ***ends*** , and it induces a second 180.degree. rotation which restores correct base-pairing at the overlap, giving the four-noded product. Correct base-pairing is not essential for religation, but may be important for release of the products. Characteristic patterns of 4, 6, 8 and 10 node knots, or 4, 8, 12 and 16 node knots were obtained, depending on the reaction conditions and the ***resolvase*** . Two pathways for multiple rounds of rotation in 360.degree. steps are inferred. The results support a model for strand exchange by supercoil-directed subunit rotation within a ***resolvase*** tetramer.

L6 ANSWER 22 OF 31 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97043066 EMBASE
DOCUMENT NUMBER: 1997043066
TITLE: TRF1, a mammalian telomeric protein.
AUTHOR: Smith S.; De Lange T.
CORPORATE SOURCE: S. Smith, Rockefeller University, 1230 York Avenue, New York, NY 10021, United States
SOURCE: Trends in Genetics, (1997) 13/1 (21-26).
Refs: 44
ISSN: 0168-9525 CODEN: TRGEE2
PUBLISHER IDENT.: S 0168-9525(96)10052-4
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 021 Developmental Biology and Teratology
022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB ***Telomerase*** ***adds*** TTAGGG repeats onto mammalian chromosome ***ends*** , replenishing the terminal sequence loss incurred during DNA replication. This maintenance of telomeric DNA

preserves binding sites for telomeric proteins, which form a protective nucleoprotein complex at chromosome ends. The recent isolation of TRF1, the mammalian telomeric-repeat binding factor, should now allow the structure and function of the telomeric complex to be examined in detail.

L6 ANSWER 23 OF 31 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95326570 EMBASE
DOCUMENT NUMBER: 1995326570
TITLE: You haven't heard the ***end*** of it: Telomere loss may ***link*** human aging with cancer.
AUTHOR: Shay J.W.; Werbin H.; Wright W.E.
CORPORATE SOURCE: Dept. of Cell Biology/Neuroscience, Univ. of Texas
Southwestern Med.Ctr., 5323 Harry Hines Boulevard,Dallas, TX 75235-9039, United States
SOURCE: Canadian Journal on Aging, (1995) 14/3 (511-524).
ISSN: 0714-9808 CODEN: CJAGE7
COUNTRY: Canada
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
020 Gerontology and Geriatrics
021 Developmental Biology and Teratology
022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English; French
AB The molecular details of the relationship between cellular senescence and
cancer are beginning to emerge. Since telomeres (the ends of the chromosomes) shorten progressively with each cell division, it has been proposed that telomere shortening is the clock that times cellular senescence. The re-expression of ***telomerase*** , the enzyme that maintains telomeres and prevents their shortening, occurs in most tumor cells and is probably a critical event in the formation and sustained growth of most cancers.

L6 ANSWER 24 OF 31 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 93155551 EMBASE
DOCUMENT NUMBER: 1993155551
TITLE: Isolation of telomeric DNA from the filamentous fungus Podospora anserina and construction of a self-replicating linear plasmid showing high transformation frequency.
AUTHOR: Javerzat J.-P.; Bhattacherjee V.; Barreau C.
CORPORATE SOURCE: Laboratoire de Genetique, UA CNRS 542, Universite de
Bordeaux II, Avenue des Facultes,33405 Talence Cedex, France
SOURCE: Nucleic Acids Research, (1993) 21/3 (497-504).
ISSN: 0305-1048 CODEN: NARHAD
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English
AB It has been previously shown that linear plasmids bearing Tetrahymena telomeric sequences are able to replicate autonomously in the filamentous fungus Podospora anserina (1). However, autonomous replication occurs in
only 50-70% of the transformants, suggesting a defect in the recognition of the Tetrahymena telomeric template by the putative P. anserina ***telomerase*** so that only a fraction of entering DNA is stabilized into linear extrachromosomal molecules. We have cloned DNA sequences ***added*** to the Tetrahymena (T2G4)(n) ***ends*** of the linear plasmid. Nucleotide sequencing showed that these sequences are exclusively
composed of T2AG3 repeat units. Hybridization experiments of Bal31 treated
DNA showed that T2AG3 repeats are confined within 200 bp in chromosomal P.
anserina telomeres. A new plasmid has been constructed so that after linearization, the terminal sequences contain T2AG3 repeats. This linear molecule transforms P. anserina with a high frequency (up to 1.75 x 104 transformants/.mu.g), autonomous replication occurs in 100% of the transformants and the plasmid copy number is about 2-3 per nucleus. These
results underscore the importance of the telomeric repeat nucleotide sequence for efficient recognition as functional telomeric DNA in vivo and provide the first step toward the development of an artificial chromosome cloning system for filamentous fungi.

L6 ANSWER 25 OF 31 MEDLINE
ACCESSION NUMBER: 1998019034 MEDLINE
DOCUMENT NUMBER: 98019034 PubMed ID: 9358002
TITLE: Developmental regulation of ***telomerase*** activity in human fetal tissues during gestation.
AUTHOR: Ulaner G A; Giudice L C
CORPORATE SOURCE: Department of Gynecology and Obstetrics, Stanford
University Medical Center, CA 94305, USA.
CONTRACT NUMBER: 5T32CA09302 (NCI)
SOURCE: MOLECULAR HUMAN REPRODUCTION, ***(1997 Sep)*** 3 (9)
769-73.
Journal code: 9513710. ISSN: 1360-9947.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 19980109
Last Updated on STN: 19980109
Entered Medline: 19971212
AB ***Telomerase*** is a ribonucleoprotein that ***adds*** hexanucleotide repeats (telomeres) to the ***ends*** of linear chromosomes, compensating for the loss of telomeric DNA which occurs with
DNA replication. In humans, ***telomerase*** has been previously detected in germ-line tissues, blastocysts, 16-20 week old fetal tissue, and most cancers, but not in mature sperm or ova, or in most normal somatic tissues. It has been hypothesized that ***telomerase*** is suppressed during somatic development and reactivated in malignancy. To test the hypothesis that ***telomerase*** is suppressed during somatic development, human fetal tissues of 8-21 weeks gestational age were assayed for ***telomerase*** activity. All tissues expressed ***telomerase*** at the earliest ages examined. Lung, liver, spleen, and testis maintained ***telomerase*** activity through the latest age assayed, namely 21 weeks. Brain and kidney ***telomerase*** activity was present up to the 16th week and was undetectable thereafter. Heart tissue did not display activity beyond the 12th week. Lysates of heart, brain, and kidney without ***telomerase*** activity did not inhibit the activity of known ***telomerase*** -positive cells, suggesting that suppression of ***telomerase*** activity during gestational development is due to a lack of active ***telomerase*** rather than to the presence of an inhibitor. These findings demonstrate tissue-specific and developmental regulation of ***telomerase*** in the human fetus, suggesting an important role for this ribonucleoprotein in human fetal tissue differentiation and development.

L6 ANSWER 26 OF 31 MEDLINE
ACCESSION NUMBER: 91054430 MEDLINE
DOCUMENT NUMBER: 91054430 PubMed ID: 2241933
TITLE: Telomeres, ***telomerase*** and senescence.
AUTHOR: Greider C W
CORPORATE SOURCE: Cold Spring Harbor Laboratory, New York 11724.
CONTRACT NUMBER: GM43080-01 (NIGMS)
SOURCE: BIOESSAYS, ***(1990 Aug)*** 12 (8) 363-9. Ref: 58
Journal code: 8510851. ISSN: 0265-9247.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199012
ENTRY DATE: Entered STN: 19910208
Last Updated on STN: 19980206
Entered Medline: 19901205
AB Eukaryotic chromosomes end with tandem repeats of simple sequences. These
GC rich repeats allow telomere replication and stabilize chromosome ends.
Telomere replication involves an equilibrium of sequence loss and addition at the ***ends*** of chromosomes. Repeats are ***added*** de

novo
by ***telomerase*** , an unusual DNA polymerase.
Telomerase
is an RNP in which an essential RNA component provides the template for
the added telomere repeats. Telomere length maintenance plays an essential
role in cell viability.

L6 ANSWER 27 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:1340 HCAPLUS
DOCUMENT NUMBER: 128:85174
TITLE: Cloning and sequences of ***telomerase*** genes from Saccharomyces cerevisiae
INVENTOR(S): Gottschling, Daniel E.; Singer, Miriam S.
PATENT ASSIGNEE(S): Arch Development Corp., USA
SOURCE: U.S., 97 pp., Cont.-in-part of U.S. Ser. No. 326,781, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5698686	A	19971216	US 1995-431080	19950428 <--
WO 9612811	A2	19960502	WO 1995-US13801	19951020 <--
WO 9612811	A3	19960801		

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT, UA
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9642786	A1	19960515	AU 1996-42786	19951020 <--
US 5916752	A	19990629	US 1997-938534	19970926
US 6387619	B1	20020514	US 1999-345294	19990630

PRIORITY APPLN. INFO.: US 1994-326781 B2 19941020
US 1995-431080 A 19950428
WO 1995-US13801 W 19951020
US 1997-938534 A3 19970926
AB Disclosed are cDNAs for the template RNA of S. cerevisiae ***telomerase*** and various ***telomerase*** -assocd. polypeptides.
Telomerase is a ribonucleoprotein enzyme that elongates the G-rich strand of chromosomal ***termini*** by ***adding*** telomeric repeats. A novel screening method was used to identify genes in S. cerevisiae that, when expressed at high levels, suppress telomeric silencing. This screen led to the identification of the gene TLC1 (***telomerase*** component 1), which codes for the template RNA component of the ribonucleoprotein enzyme, as well as 5 new genes (Suppressors of Telomeric Repression genes STR1 and STR3-6) encoding ***telomerase*** -assocd. proteins. The nucleotide sequences of the genes and deduced amino acid sequences of the proteins are provided. Gene
TLC1 was mapped to a single site on chromosome II, immediately adjacent to
CSG2.

L6 ANSWER 28 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:401846 HCAPLUS
DOCUMENT NUMBER: 125:50804
TITLE: Cloning and sequences of ***telomerase*** genes from Saccharomyces cerevisiae
INVENTOR(S): Gottschling, Daniel E.; Singer, Miriam S.
PATENT ASSIGNEE(S): Arch Development Corporation, USA
SOURCE: PCT Int. Appl., 347 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9612811	A2	19960502	WO 1995-US13801	19951020 <--
WO 9612811	A3	19960801		

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT, UA
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

US 5698686	A	19971216	US 1995-431080	19950428 <--
AU 9642786	A1	19960515	AU 1996-42786	19951020 <--

PRIORITY APPLN. INFO.: US 1994-326781 A 19941020
US 1995-431080 A 19950428
WO 1995-US13801 W 19951020
AB ***Telomerase*** is a ribonucleoprotein enzyme that elongates the G-rich strand of chromosomal ***termini*** by ***adding*** telomeric repeats. A novel screening method was used to identify genes in S. cerevisiae that, when expressed at high levels, suppress telomeric silencing. This screen leads to the identification of the gene TLC1 (***telomerase*** component 1), which codes for the template RNA component of the ribonucleoprotein enzyme, as well as 5 new genes encoding ***telomerase*** -assocd. proteins. The nucleotide sequences of the genes and deduced amino acid sequences of the proteins are provided. Also disclosed are various methods, compns., and screening assays connected with ***telomerase*** , including genes encoding the template RNA of S. cerevisiae ***telomerase*** and various ***telomerase*** -assocd. polypeptides.

L6 ANSWER 29 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:237587 HCAPLUS
DOCUMENT NUMBER: 120:237587
TITLE: Methods for the isothermal amplification of nucleic acid molecules
INVENTOR(S): Auerbach, Jeffrey I.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9403624	A1	19940217	WO 1993-US7309	19930804 <--

W: CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

US 6218152	B1	20010417	US 1998-188214	19981109
US 6261808	B1	20010717	US 2000-657943	20000908
US 2002102575	A1	20020801	US 2001-899834	20010709

PRIORITY APPLN. INFO.: US 1992-924643 A 19920804
US 1992-933945 A2 19920824
WO 1993-US7309 A2 19930804
US 1995-383327 A2 19950203
US 1995-533852 A2 19950926
US 1996-595226 A2 19960201
US 1997-906491 A1 19970805
US 1998-188214 A2 19981109
US 2000-657943 A1 20000908
AB Methods for amplifying a nucleic acid mol. using a single prime under isothermal conditions are described. The method leads to the formation of a twin origin "rolling circle" replication intermediate that results from the extension of two primers during the amplification of a single-stranded circular mol. The method involves primer-dependent. prepn. of a copy of

the target sequence followed by modification of the 3'terminus of the copy with an inverted repeat sequence that is then used as a primer to extend the mol. in the other direction. One of the ***termini*** is then ***ligated*** with a nucleic acid contg. a recombination site such as loxP and a ***recombinase*** is then used to form a circular mol. that is amplified from the primer. Several variations of the method are described.

L6 ANSWER 30 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:566787 HCAPLUS
DOCUMENT NUMBER: 113:166787
TITLE: Overproduction of human immunodeficiency virus type I reverse transcriptase in Escherichia coli and purification of the enzyme
AUTHOR(S): Saitoh, Atsushi; Iwasaki, Hiroshi; Nakata, Atsuo; Adachi, Akio; Shinagawa, Hideo
CORPORATE SOURCE: Res. Inst. Microb. Dis., Osaka Univ., Suita, 565, Japan
SOURCE: Microbiol. Immunol. (***1990***), 34(6), 509-21
CODEN: MIIMDV; ISSN: 0385-5600
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Overexpression of the reverse transcriptase was designed in E. coli. For a high level of expression, HIV protein was expressed as a protein fusion with .beta.-galactosidase. When the proviral DNA fragment covering the 3' half of the gag gene and the entire pol gene was ***ligated*** to the 3' ***end*** of the lacZ gene to fuse the truncated gag to lacZ in frame, a small quantity of reverse transcriptase was produced, indicating that frameshifting and post-translational processing have occurred. Much more reverse transcriptase was produced when the entire pol region was directly fused to the lacZ gene. From a 1 L culture of bacteria, 1 mg of highly purified reverse transcriptase consisting of approx. equimolar amts. of 2 species (p64 and p51) was obtained. These proteins had identical N-termini consistent with the deduced amino acid sequence and therefore, might be correctly processed from the fusion protein in E. coli by the protease encoded by the pol region. The purified reverse transcriptase was enzymically as active as the enzyme purified from the virus particles, and immunoreactive to the sera of HIV carriers with high sensitivity and specificity.

L6 ANSWER 31 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:436768 HCAPLUS
DOCUMENT NUMBER: 113:36768
TITLE: Reverse transcriptase, the end of the chromosome, and the end of life
AUTHOR(S): Boeke, Jef D.
CORPORATE SOURCE: Sch. Med., Johns Hopkins Univ., Baltimore, MD, 21205, USA
SOURCE: Cell (Cambridge, Mass.) (***1990***), 61(2), 193-5
CODEN: CELLB5; ISSN: 0092-8674
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 16 refs., of the function of reverse transcriptases, esp. the role of ***telomerases*** in ***adding*** telomeric repeats to chromosome ***ends*** . The relation between senescence and altered telomer structure is discussed.